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09/578,507

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Natarajan Ramasubramanyan

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7987

7590

03/05/2002

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EXAMINER

SANDALS, WILLIAM O

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 03/05/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
09/578,507

Applicant(s)  
Ramasubramanyan

Examiner  
William Sandals

Art Unit  
1636



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Feb 2, 2002
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-53 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-53 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: \_\_\_\_\_

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## DETAILED ACTION

### *Response to Arguments*

1. Amendments to the claims and specification in Paper No. 9, filed January 2, 2002 have overcome the rejections of the claims under 35 USC 112, second paragraph in the previous office action, and the rejections are withdrawn.
2. Arguments regarding the claims in Paper No. 9 have overcome the rejections of the claims under 35 USC 102 and 103 in the previous office action, and the rejections are withdrawn.
3. Amendments to the specification in Paper No. 9 have overcome the objection of the claims in the previous office action, and the objection is withdrawn.
4. Applicant's arguments with respect to claims 1-53 have been considered but are moot in view of the new ground(s) of rejection.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

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claimed invention. Claim 1 has been amended in Paper No. 9 to recite in line 10 “in the absence of non-aqueous solvents”. The genus of non-aqueous solvents is not described in the claims or specification in a way to convey a clear definition of the genus. The term “non-aqueous solvents” is not found in the specification. A few examples of solvents are given in the specification, but they do not provide a working understanding of what may be included in the genus “non-aqueous solvents”. The scope of the genus includes many types of solvents, and the genus is widely variant since some solvents may be classified as aqueous under some conditions and non-aqueous under other conditions. No common structural or functional attributes identify members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general knowledge guidance is what is needed. Since the disclosure fails to describe the common structural or functional attributes or characteristics of the members of the genus, and because the members of the genus are highly variant, the “non-aqueous solvent” referred to in the claim is insufficient to describe the products used in the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of non-aqueous solvents to describe the genus. Thus, applicant was not in possession of the claimed genus.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 1-16 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
9. Claim 1 recites the term “absence of non-aqueous solvents”. “Absence of non-aqueous solvents” is not defined in the specification or claims. Without proper guidance as to the meaning of the term, one of ordinary skill in the art would not know the metes and bounds of the claim.
10. Claims 14-15 and 44-45 are rejected. Claims 14 and 44 recite “wherein the hydrophobic interaction media are selected from the group consisting of a methacrylate polymer or copolymer backbone bound to at least one of...”. Claims 15 and 45 depend from claims 14 and 44 respectively and claims 15 and 45 recite “wherein the media is at least one of a methacrylate ethylene glycol copolymer backbone or a cross-linked agarose backbone”. Nowhere does claims 14 or 44 include the opportunity for a “methacrylate ethylene glycol copolymer backbone” or a cross-linked agarose backbone” to be permitted in the base structure, since the “methacrylate ethylene glycol copolymer backbone” or “cross-linked agarose backbone” are chemically distinct from the base claimed “methacrylate polymer or copolymer backbone”, and are not encompassed by the meaning of a “methacrylate polymer or copolymer backbone”. The addition of this limitation at this point in the claim structure makes the intended meaning of the base claims 14 and 44 unclear. Claims 14-15 and 44-45 are thus vague and indefinite.

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***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. Claims 1-6, 10-25, 29-46 and 49-53 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2001/0034435 A1.

US 2001/0034435 A1 taught (see especially paragraphs 21-23, 27, 32-34, 46 and 52-56 and the claims) a method for purifying plasmid DNA from a mixture containing at least one impurity by binding the mixture to a hydrophobic interaction media, and eluting the plasmid with a salt (ammonium sulfate, 1M-2M) solution at a pH of 5.5-9. The impurity is RNA, endotoxin or chromosomal DNA. The hydrophobic interaction media comprises a chromatography support with pendent hydrophobic groups consisting of C3 to C10 alkyl groups (propyl thru decyl). The chromatography media is in the form of an agarose cross-linked backbone bead in the size range of 15-100  $\mu$ m. The method separates supercoiled plasmid from relaxed plasmid, and also separates plasmid from endotoxin.

***Claim Rejections - 35 USC § 103***

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13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 1-25, 29-46 and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2001/0034435 A1 in view of El Rassi et al. (of record).

The claims are drawn to a method for purifying plasmid DNA from a mixture containing at least one impurity by binding the mixture to a hydrophobic interaction media, and eluting the plasmid with a salt (ammonium sulfate, 1M-2M or sodium chloride, 2M-4M) solution at a pH of 5.5-9. The impurity is RNA, endotoxin or chromosomal DNA. The hydrophobic interaction media comprises a chromatography support with pendent hydrophobic groups consisting of C3 to C10 alkyl groups (propyl thru decyl). The chromatography media is in the form of an agarose cross-linked backbone bead in the size range of 15-100  $\mu$ m. The method separates supercoiled plasmid from relaxed plasmid, and also separates plasmid from endotoxin.

US 2001/0034435 A1 taught the method as described above in the rejection under 35 USC 102.

US 2001/0034435 A1 did not teach that the sodium chloride was 2M-4M.

El Rassi et al. taught (see especially the figures) the use of ammonium sulfate or sodium chloride in hydrophobic interaction chromatography in a range of 2M-4M were equivalent for the purposes of eluting bound molecules from hydrophobic interaction media.

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It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of US 2001/0034435 A1 with El Rassi et al. to produce the instant invention because El Rassi et al. taught the practical and theoretical aspects of hydrophobic interaction chromatography (HIC), showing the general and desirable use of sodium chloride at concentrations of 2M-4M as an equivalent salt to ammonium sulfate, for elution of macromolecules with HIC.

One of ordinary skill in the art would have been motivated to combine the teachings of US 2001/0034435 A1 with El Rassi et al. to produce the instant invention because El Rassi et al. explain the theory of hydrophobic interaction chromatography as it applies to salt concentration, showing that the retention of molecules which bind to the hydrophobic interaction chromatography media decreases as the salt concentration decreases (explained as a function of the surface tension of the salt solution). El Rassi et al. demonstrate that sodium chloride in the range of 2M-4M was a useful and desirable equivalence to ammonium sulfate, as used in US 2001/0034435 A1. US 2001/0034435 A1 suggests the use of sodium chloride for producing elution of molecules from the hydrophobic interaction chromatography media at paragraph 27. Given the suggestion to use sodium chloride in US 2001/0034435 A1 and the teaching of equivalence of sodium chloride in El Rassi et al. one of ordinary skill in the art would certainly have been motivated to use sodium chloride in a method of hydrophobic interaction chromatography. Further, a person of ordinary skill in the art would have had a reasonable



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expectation of success in the producing the instant claimed invention given the teachings of US 2001/0034435 A1 with El Rassi et al.

15. Claims 1-53 rejected under 35 U.S.C. 103(a) as being unpatentable over US 2001/0034435 A1 in view of El Rassi et al. as applied to claims 1-25, 29-46 and 49-53 above, and further in view of Ishida et al (of record).

The claims are drawn to the invention as described above and also where the ammonium sulfate concentration is about 2.5M-4M or about 2.35M-2.45M.

US 2001/0034435 A1 in view of El Rassi et al. taught the invention as described above.

US 2001/0034435 A1 in view of El Rassi et al. did not teach that the ammonium sulfate concentration is about 2.5M-4M.

Ishida et al. taught (see especially the figures) hydrophobic interaction chromatography using either sodium chloride or ammonium sulfate, where the concentration of ammonium sulfate was used in the concentration ranges of 0-2.5M to remove endotoxin from therapeutic preparations which have high endotoxin levels.

It would have been obvious to one of ordinary skill in the art at the time of filing the instant application to combine the teachings of US 2001/0034435 A1 and El Rassi et al. with Ishida et al. to produce the instant invention because Ishida et al. taught the separation of endotoxin from therapeutic preparations with hydrophobic interaction chromatography, as did US 2001/0034435 A1.

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One of ordinary skill in the art would have been motivated to combine the teachings of US 2001/0034435 A1 and El Rassi et al. with Ishida et al. to produce the instant invention because Ishida et al. taught that the use of hydrophobic interaction chromatography for the removal of endotoxin from a preparation was greatly improved over existing technology, as did US 2001/0034435 A1. Ishida et al. showed that endotoxin was strongly bound to the hydrophobic interaction chromatography media at ammonium sulfate concentrations of up to 2.5M, demonstrating the desirable and beneficial use of hydrophobic interaction chromatography with ammonium sulfate concentrations up to 2.5M in the instant claimed method. US 2001/0034435 A1 taught the desirable use of ammonium sulfate, preferably above 1.6M for plasmid separation and endotoxin removal methods. Thus one of ordinary skill in the art would have been motivated to combine the teachings of Ishida et al. and US 2001/0034435 A1 make the instant invention for the beneficial and desirable removal of endotoxin from therapeutic preparations. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant US 2001/0034435 A1, El Rassi et al. and Ishida et al.

### ***Conclusion***

16. Certain papers related to this application are *welcomed* to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61

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(November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Zeta Adams, whose telephone number is (703) 305-3291.

William Sandals, Ph.D.

Examiner

February 26, 2002

